Desmosome

Identification of Desmoglein as a Cadherin and Analysis of Desmoglein Domain Structure

Ken Ishii[1]

[1]Department of Dermatology, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Correspondence: Dr Ken Ishii, E-mail: kishii@mail.med.upenn.edu

Published online 30 January 2007. doi:10.1038/sj.skinbio.6250001

In the 1980s and early 1990s, the ability to clone complementary DNA (cDNA) resulted in great advances in cell biology, including our understanding of cell adhesion. Cloning the cDNA encoding desmosomal molecules, and the determination of their deduced amino-acid sequences, provided novel insights into their structure and function.

It had been shown by various biochemical and immunochemical techniques that desmosomal proteins consist of plaque proteins inside the cell and transmembrane glycoproteins. For desmosomal transmembrane glycoproteins, Koch *et al*. (1990) first isolated and characterized the cDNA encoding desmoglein in 1990. Using monoclonal antibodies against desmoglein, they screened cDNA expression libraries constructed from bovine muzzle epithelial mRNA. The major scientific advance from this work was that the deduced amino-acid sequences of their isolated clones showed high homology to cadherins, which had already been shown to be calcium-dependent cell adhesion molecules. Thus, they identified desmoglein as a member of the cadherin supergene family of cell adhesion molecules.

Similar to classic cadherins such as E- and N-cadherins, they, and subsequently others, showed that desmoglein is a type I transmembrane protein with an amino-terminal extracellular domain, a single transmembrane spanning region, and a carboxy-terminal cytoplasmic domain (Figure 1). The extracellular domain was shown to contain four subdomain repeating units that have homology to similar extracellular subdomains in cadherins and that, similar to those units, contained putative calcium-binding sites. The cytoplasmic domain of desmoglein, although it contained a subdomain (termed the intracellular cadherin segment or ICS) that was homologous to a cytoplasmic subdomain of cadherin, significantly differed in that it was longer than that of cadherins. In addition to the ICS subdomain, desmoglein contained a proline-rich linker (IPL) and a terminal repeating unit domain (RUD). Although the ICS domain has been shown to bind various intracellular molecules, such as plakoglobin, the function of the additional subdomains of desmoglein remains unclear.

Progress, by cDNA cloning, was also made in characterizing the other major transmembrane molecule of the desmosome, desmocollin (Collins *et al*., 1991). cDNA cloning of desmocollin indicated that it also belonged to the cadherin family. The unique aspect of desmocollin was that the cytoplasmic domain contained a longer "a" form and a shorter "b" form, produced by alternative splicing of mRNA.

To date, four isoforms of desmoglein (Dsg1–4) and three isoforms of desmocollin (Dsc1–3) have been identified, each arising from a different gene. The genes are clustered on the q arm of chromosome 18 for humans (Kljuic *et al*., 2003). Because of their homologies to classical cadherins, these glycoproteins are now termed "desmosomal cadherins".

The cDNA cloning of desmogleins and, subsequently, desmocollins,

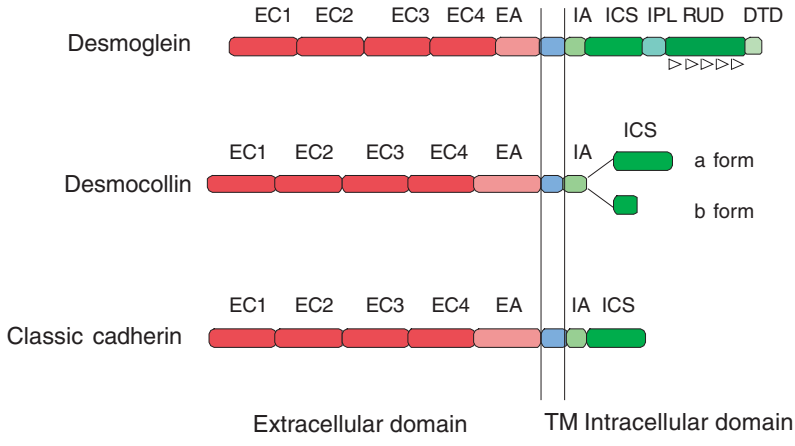

Figure 1. Structure of desmosomal cadherins (desmoglein and the two splice forms of desmocollin) and the classical cadherin E-cadherin. EC1–EC4, four extracellular cadherin-typical repeats; EA, extracellular anchor domain; TM, transmembrane domain; IA, intracellular anchor domain; ICS, intracellular cadherin-specific domain. Desmoglein contains an additional intracellular domain: IPL, proline-rich linker domain; RUD, repeating unit domain; DTD, desmoglein-specific terminal domain. (Adapted from Amagai, 1996, with permission from Elsevier.)

provided the first evidence that these molecules could be calcium-dependent cell adhesion molecules and might provide the adhesive component of desmosomes. Their cloning provided cell biologists the tools necessary to test these hypotheses directly and to study the involvement of these desmosomal cadherins in disease.

ACKNOWLEDGMENT
I am grateful to Dr. John Stanley for helpful comments.

TO CITE THIS ARTICLE

Ishii K (2007) Identification of desmoglein as a cadherin and analysis of desmoglein domain structure. *J Invest Dermatol* 127:E6–7

REFERENCES

Amagai M (1996) Pemphigus: autoimmunity to epidermal cell adhesion molecules. *Adv Dermatol* 11:319–52

Collins JE, Legan PK, Kenny TP, MacGarvie J, Holton JL, Garrod DR (1991) Cloning and sequence analysis of desmosomal glycoproteins 2 and 3 (desmocollins): cadherin-like desmosomal adhesion molecules with heterogeneous cytoplasmic domains. *J Cell Biol* 113:381–91

Kljuic A, Bazzi H, Sundberg JP, Martinez-Mir A, O'Shaughnessy R, Mahoney MG *et al.* (2003) Desmoglein 4 in hair follicle differentiation and epidermal adhesion: evidence from inherited hypotrichosis and acquired pemphigus vulgaris. *Cell* 113:249–60

Koch PJ, Walsh MJ, Schmelz M, Goldschmidt MD, Zimbelmann R, Franke WW (1990). Identification of desmoglein, a constitutive desmosomal glycoprotein, as a member of the cadherin family of cell adhesion molecules. *Eur J Cell Biol* 53:1–12.